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CLAIMS

1. Transduced hepatocytes, comprising incorporated genetic material.
- 05 2. Genetically modified hepatocytes of Claim 1 wherein the incorporated genetic material is genetic material of interest comprising:
  - 10 a. genetic material present in and expressed at biologically effective levels by normal hepatocytes, but present in or expressed in less than normal quantities in the hepatocytes prior to stable transfer of genetic material of interest into them;
  - b. genetic material not present in normal hepatocytes; or
  - 15 c. genetic material present in normal hepatocytes but not expressed at biologically effective levels in such cells, alone or in any combination thereof.
- 20 3. Transduced hepatocytes of Claim 2, additionally comprising genetic material encoding a selectable marker.
4. Hepatocytes infected with a viral vector which has a recombinant genome, the recombinant genome comprising incorporated genetic material.
- 25 5. Hepatocytes of Claim 4 in which the incorporated genetic material is:

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- 05           a.   genetic material present in and expressed at  
              biologically effective levels by normal hepato-  
              cytes, but present in or expressed in less than  
              normal quantities in the hepatocytes prior to  
              stable transfer of genetic material of interest  
              into them;
- b.   genetic material not present in normal hepato-  
              cytes; or
- 10           c.   genetic material present in normal hepatocytes  
              but not expressed at biologically effective  
              levels in such cells, alone or in any combina-  
              tion thereof.
- 15           6.   Hepatocytes of Claim 5, wherein the incorporated  
              genetic material additionally comprises genetic  
              material encoding at least one selectable marker.
7.   Hepatocytes of Claim 6 in which at least one select-  
              able marker is a gene encoding antibiotic resistance  
              or a gene that complements a genetic defect in the  
              host species.
- 20           8.   Hepatocytes of Claim 7 in which the gene encoding  
              antibiotic resistance is the neo gene and the gene  
              encoding an essential product is the his D gene.
- 25           9.   Human hepatocytes of Claim 5 in which the incorpo-  
              rated genetic material encodes a hormone, an enzyme  
              or a drug.

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10. Human hepatocytes capable of expressing incorporated genetic material, the incorporated genetic material selected from the group consisting of:
  - 05 a. genetic material present in and expressed at biologically effective levels by normal hepatocytes, but present in or expressed in less than normal quantities in the hepatocytes prior to stable transfer of genetic material of interest into them;
  - 10 b. genetic material not present in normal hepatocytes; or
  - 15 c. genetic material present in normal hepatocytes but not expressed at biologically effective levels in such cells, alone or in any combination thereof.
11. Hepatocytes having incorporated therein recombinant amphotropic retrovirus having a recombinant genome comprised of:
  - 20 a. long terminal repeat sequences, the tRNA binding site and the Psi packing site derived from amphotropic Moloney murine leukemia virus; and
  - b. genetic material encoding at least one polypeptide of interest.
12. Hepatocytes of Claim 11 in which the recombinant  
25 genome additionally comprises genetic material encoding at least one selectable marker.
13. Hepatocytes of Claim 13 in which the genetic material encoding at least one selectable marker is a neo gene.

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14. Hepatocytes of Claim 14 in which the genetic material encodes human low density lipoprotein receptor.
- 05 15. Transduced hepatocytes capable of episomal expression of incorporated genetic material.
16. A method of making transduced hepatocytes comprising incorporated genetic material which encodes at least one polypeptide of interest, comprising:
  - 10 a. contacting cultured hepatocytes with media containing an infectious recombinant retrovirus having a recombinant genome comprised of genetic material of interest; and
  - 15 b. maintaining the cultured hepatocytes and the media containing the infectious recombinant retrovirus under conditions appropriate for infection of the hepatocytes by recombinant retrovirus.
17. A method of Claim 16 in which the incorporated genetic material additionally comprises genetic material encoding at least one dominant selectable  
20 marker.
18. A method of making hepatocytes, capable of expressing incorporated genetic material encoding at least one protein or at least one polypeptide of interest, comprising:
  - 25 a. transducing cultured hepatocytes with genetic material encoding at least one protein or at least one polypeptide of interest and

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- b. culturing transduced hepatocytes under conditions appropriate for their growth.
19. A method of implanting genetically modified hepatocytes which express incorporated genetic material of interest in a mammal, comprising the steps of:
- a. contacting cultured hepatocytes with medium containing an infectious recombinant retrovirus having a recombinant genome comprised of genetic material of interest;
  - b. maintaining the cultured hepatocytes and the medium under conditions appropriate for infection of the hepatocytes by recombinant retrovirus; and
  - c. introducing the modified hepatocytes produced in (b) into the mammal
20. A method of implanting genetically transduced hepatocytes capable of expressing incorporated genetic material of interest in a mammal, comprising the steps of:
- a. transducing cultured hepatocytes with genetic material encoding at least one protein or at least one polypeptide of interest;
  - b. culturing transduced hepatocytes under conditions appropriate for their growth; and
  - c. introducing the transduced hepatocytes produced in (b) into the mammal.
21. A method of treating a defect in liver function which is the result of abnormal production of a

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protein or a polypeptide, comprising introducing into the liver transduced hepatocytes comprising genetic material encoding the protein or the polypeptide whose abnormal production in the hepatocyte is the cause of the defect, under conditions appropriate for expression of the protein or the polypeptide in the hepatocytes.

22. A method of providing a hormone, an enzyme or a drug to an individual, comprising transducing hepatocytes with genetic material encoding the hormone, the enzyme or the drug and introducing the transduced hepatocytes into the individual.

23. A method of providing a protein or a polypeptide normally expressed by hepatocytes to an individual in whom expression of the protein or the polypeptide is compromised, comprising:

- a. transducing hepatocytes with a recombinant retrovirus having a recombinant genome comprised of:
  - 1) genetic material encoding the protein or the polypeptide;
  - 2) the long terminal repeat sequences, the tRNA binding site and the Psi packaging site derived from an amphotropic retrovirus; and
  - 3) at least one promoter of eukaryotic origin; and
- b. introducing transduced hepatocytes into the individual.

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24. A method of Claim 23 in which the recombinant genome is additionally comprised of a promoter of eukaryotic origin which can be modulated by an external cue.
- 05 25. A method of Claim 24 in which the recombinant genome is additionally comprised of genetic material encoding at least one dominant selectable marker.
- 10 26. A method of Claim 25 in which at least one dominant selectable marker is a gene encoding antibiotic resistance or a gene that complements a genetic defect in the host species.
27. A recombinant vector for transducing hepatocytes with genetic material encoding a protein of interest or a polypeptide of interest.